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EXAMINER	
NOAKES, SUZANNE MARIE	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
05/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents-US-NY@novozymes.com

Office Action Summary	Application No.	Applicant(s)	
	10/582,277	NIELSEN ET AL.	
	Examiner	Art Unit	
	SUZANNE M. NOAKES	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41 and 46-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41 and 46-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The remarks and amendments filed 02/25/2009 in response to the previous non-final Office action are acknowledged. Applicants have cancelled claims 27-40 and 42-45 and added new claims 47-65, which are commensurate in scope with the previously examined claims. Thus claims 41 and 46-65 are pending and subject to examination on the merits.

Withdrawal of Previous Objections/Rejections

2. Any objection/rejection recited previously and not explicitly reiterated below is withdrawn.

3. The objection to claims 41 and 46 are objected to because for minor informalities such as the claims being dependent upon withdrawn, non-elected claims and the use of acronyms without recitation of what it stands for are withdrawn in view of the amendments to the claims.

4. The rejection of claims 41 and 46 under 35 USC 112 1st paragraph, scope of enablement as recited in the previous Office action, Section 7, and under written description (previous Office action, Section 8) are withdrawn in view of the limitation of the scope of genus of polypeptides encompassed by the method, e.g. SEQ ID NO: 2 and those with 90% identity thereto.

Claim Rejections - 35 USC § 112 – 1st paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 41 and 46 as currently amended, and new claims 47, 49-59 and 62-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making/enhancing the secretion of a protein of interest by cultivating cells from the genus of *Bacillus* wherein a progeny cell is derived from a parent cell and wherein said progeny cell encodes at least an MrgA protein and wherein said cells are derived from (and cultivated) the genus *Bacillus*, does not reasonably provide enablement for methods of enhancing section and/or increasing the production of a protein of interest by cultivating cells expressing MrgA and methods said proteins are expressed in any kind of cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is recited in the previous Office, Section 6.

Applicants arguments and Examiner's Rebuttal:

Applicants traverse the rejection of record and state that the Office has not established a standard of under experimentation expected of one skilled in the art in order to make and use the invention in all cells. In particular, Applicants assert that the specification described that the present disclosure relates to recombinant host cells which can can be used in the recombinant production of the proteins of interest. In

particular, the specification discloses on page 16, that the choice of host cell will to a large extent depend upon the gene encoding the polypeptide and its source. The specification also discloses that the host cell may be a unicellular microorganism, e.g., a prokaryote, or a non-unicellular microorganism, e.g., a eukaryote. Useful unicellular cells are bacterial cells such as gram positive bacteria. Further the specification includes a detailed description providing extensive disclosure of how to produce the proteins of interest, how to produce the various cells for example by fermentation, etc. and that these are routine in the art.

Applicants also state: This evidence establishes that the specification enables the claimed invention. Application of the Wands factors to these facts further supports the conclusion that the claims are enabled. First, the present invention is in the field of molecular biology. The Wands court has already held that the level of skill in this art is high. Wands, 858 F.2d at 740. Second, the specification provides an extensive disclosure for producing the claimed cells. Third, as in Wands, the methods of making the claimed cells and screening for the recombinant nature there are known in the art. Fourth, the specification provides working examples of several many different strains of Bacillus subtiilis. Fifth, given the extensive guidance given in the specification and the high level of skill in the art, the experimentation involved to produce other cells within the scope of the claims is routine and well within the skill of those in the art. As held by the Wands court, "The test is not merely quantitative since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experiment should proceed." Id. at 737. (see Remarks, p. 8, 3rd paragraph).

However, this is not deemed persuasive to overcome the rejection of record. As stated previously, the description of how to make and use the claimed invention in

anything other than Bacillus is generic at best. While one skilled in the art is equipped to perform such routine tasks, this does not compensate for the fact that Applicants have merely provided a best guestimate that this might work in other organisms. In addition, Applicants say nothing about the predictability of said skilled aritsan ever being able to make and use the invention within the broad scope of the claims. For instance, there would be little no expectation that this method would work in gram-negative bacteria given that their secretory pathways do not have a protein that is remotely homologous to MrgA. The secretory pathways in eukaryotes is riddled with even greater uncertainty because of the enormous amount of different secretory pathways and proteins/enzymes involved therein. Furthermore, the prior art is completely silent with respect to the fact the MrgA is even involved in secretory pathways (thus leading to greater production of proteins of interest), and if one is not apprised to where or how it functions, one skilled in the art will have little knowledge or clues as to which host cells would work and which would not. While a certain amount of routine experimentation is certainly within the realms of the enablement statute, what is not expected is for the skilled artisan to actually have to figure out Applicants claimed invention having been given a sketchy road map to navigate with. As noted in the previous Office action and is apparent given that claims 48 and 60 and not included in the instant rejection, the claims are deemed enabled for those host cells within the genus of *Bacillus*.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 41 and 46-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Mol. Micro., 1995, cited on IDS).

Chen et al. teach a strain of parent cells known as MA991 which are hydrogen peroxide sensitive cells that constitutively express catalase (KatA) and alkyl hydrogen peroxide reductases (AhpC and AhpF), as well as two other proteins of 113 kDa and 16kDa. Chen et al. transformed these cells (MA991) by inserting the heterologous genes *mrgA-lacZ* to express said MrgA and beta-galactosidase proteins, thus resulting in progeny cells (strain HB1032 - a *Bacillus subtilis* strain – meets claims 47-48 and 59-60) – See p. 297, 1st column, paragraphs 1-2. It was noted that N-terminal sequencing indicated that the 113 kDa and 16 kDa protein over expressed in MA991 and thus HB1032 was identical to, and thus, MrgA (the former being in oligormeric complex the later a monomer - See p. 297, 1st column, paragraph 2) and the sequence for the MrgA is show in Figure 1, it is ntoed said sequence is 100% identical to the instant SEQ ID NO: 2 (thus, meets claims 41, 46, 51-58, 63-65. It is further noted that lacZ, e.g. a protein of interest, produces a beta-galatosidase (e.g. meets claims 50 and 62). Thus, strain HB1032 possesses at least two copies of MrgA (e.g. one naturally occurring in the parent strain, the other having been introduced into the progeny cell). Simple

induction of the MrgA-LacZ fusion creates a progeny cell that produces significantly more MrgA AND LacZ than the parent strain. Thus, this meets the limitations of the claims.

Examiners Arguments and Examiner's Rebuttal:

Applicants traverse the rejection and state: Nowhere does Chen describe progeny cells that produce greater amounts of the claimed MrgA than the parent call AND greater amounts of the protein of interest than the parent cell.

The Examiner, however, disagrees. The progeny cell has been designed to overproduce an MrgA-LacZ fusion protein. Thus, the protein of interest is LacZ. The simple induction and overexpression of this fusion construct necessarily results in an overproduction of BOTH the LacZ and the MrgA proteins (see p. 296, wherein *MrgA-lacZ* expression was induced 6-10 fold). Thus, this meets the limitation of the claims. Since it is known and even stated in the specification that *Bacillus subtilis* inherently produces MrgA, then inserting the MrgA-LacZ fusion construct necessarily and inherently means that the progeny cell has at least one copy of said MrgA gene being over produced and even has two copies of said gene. It is further noted that the sequence listed in Figure 1 for the MrgA protein is identical to the instant SEQ ID NO: 2.

New Objections/Rejections

Claim Objections

9. Claims 41 and 46 and those that depend therefrom are objected to because of the following informalities: The claims can be improved with respect to form.

a) It is noted that the claims states that the amino acid sequence is at least 90% identical to SEQ ID NO: 2. However, it is noted that something is either identical or it is not. However, something can have degrees of *identity* such as 90%. The examiner suggest modifying the claim to read that 'the amino acid sequence has at least 90% identity'.

b) The "and/or" portion of claim a) renders the claim slightly confusing and awkward. The examiner suggests modifying the claim such as: '...which has at least 90% identity to SEQ ID NO: 2 and, optionally, further comprising a DNA segment operably linked thereto, wherein said gene and/or DNA segment is manipulated.....".

Appropriate correction is required.

Conclusion

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
14 May 2009